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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/276,268	03/25/99	STRACHAN L	11000/1037

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EXAMINER	
DECLOUX, A	

ART UNIT	PAPER NUMBER
1644	8

DATE MAILED: 04/20/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/276,268	Strachan et al.
Examiner	**Group Art Unit**
DeCloux, Amy	1644

☒ Responsive to communication(s) filed on *Mar 20, 2000*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-19* is/are pending in the application.

Of the above, claim(s) *1, 2, 9, 10, and 12-19* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *3-8, and 11* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *5*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Applicant's election of Group II, Claims 3-8 and 11, species SEQ ID NO:4 in Paper No. 7 (3-20-00) is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election witerse acknowledged. Accordingly, claims 1-2, 9-10 and 12-19 stand withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a nonelected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

2. The specification is objected to because incorporation of subject matter into the patent application by reference to a hyperlink and/or other forms of browser-executable code is considered to be an improper incorporation by reference. See MPEP 608.01(p), paragraph I regarding incorporation by reference. Therefore the embedded hyperlinks and/or other forms of browser-executable code disclosed on page 7 of the instant specification are impermissible and require deletion. Where the hyperlinks and/or other forms of browser-executable codes are part of applicant's invention and are necessary to be included in the patent application in order to comply with the requirements of 35 U.S.C. 112, first paragraph, and applicant does not intend to have these hyperlinks be active links, then this objection will be withdrawn and the Office will disable these hyperlinks when preparing the patent text to be loaded onto the PTO web database.

3. Claims 7 and 11 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim can not depend from other multiple dependent claims such as Claims 3 and 6. See MPEP § 608.01(n).

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 3-8 and 11 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial, a credible asserted utility or a well established utility.

The disclosed polynucleotides in SEQ ID NOs:1-10 and the polynucleotides which encode the polypeptides in SEQ ID Nos:11-20 do not have a substantial or a well established utility. The specification discloses that the nucleotides and polypeptides encoded by the nucleotides were isolated by high-throughput sequencing of a cDNA expression library constructed from flaky skin mice stromal cells and subtracted from a cDNA library made from 3T3 fibroblasts (see pages 15 and 16 of the instant specification).

The specification further discloses that the polynucleotides and polypeptides of the present invention are likely to have important roles in the growth and development of the immune system and can be used to treat unspecified disorders in a patient, and can be used as DNA vaccines against unspecified disorders (See pages 12 and 13 of the instant specification). However, none of these uses is a specific and substantial use. Applicant is directed to the Revised Interim Utility Guidelines, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999 (available on the PTO Website).

In addition, the Applicants have not provided any examples in the use of the polynucleotides in a manner commensurate with the disclosed uses but rather have provided a number of generic examples of the uses of a polynucleotide which encodes a polypeptide with a putative therapeutic use. However, the examiner notes that the disclosed sequences may not even be related to the disclosed immunologically related functions because the subtraction cDNA library instead of resulting from the difference between stromal cells isolated from flaky skin mice and stromal cells isolated from wildtype congenic mice, results from differences between stromal cells isolated from flaky skin mice and 3T3 cells, and accordingly non-

immunologically related sequences may result from the disclosed method of obtaining SEQ ID NO:s 1-20. No specific functions attributed to any of the SEQ ID NOs:11-20 are disclosed in the specification, with the exception of SEQ ID NO:13. The specification discloses that SEQ ID NO:13 has more than 25% homology to known members of the Tumor necrosis factor (TNF) family and is thus likely to have similar functions. Since the level of identity between SEQ ID NO:13 and TNF receptor family of proteins is not very high (about 25%) and since the state of the art has not advanced to the point of being able to unequivocally determine a protein's function based solely from the amino acid sequence, it is speculative to extrapolate that the polypeptide of SEQ ID NO:13 has similar biological functions as the functions as TNF receptor family of proteins, absence evidence to the contrary.

It is noted that the specification provides no exemplification of any biological activity for the polypeptides of SEQ ID NO: 11-20, nor does it provide specific assays for any biological activity of SEQ ID NO: 11-20. Consequently, use of the claimed invention requires carrying out further research to identify or reasonably confirm a substantial "real world" utility for the claimed invention. Accordingly, the following recitations of an isolated polypeptide or polynucleotide having at least 40%, 60%, 75% or 90% to SEQ ID NO:s 11-20 and to SEQ ID NO:s 1-10, respectively, a 200mer, 100mer or 40mer of said isolated polynucleotide, the complement, reverse complement or the reverse sequence of said isolated polynucleotide, a pharmaceutical composition of said isolated polynucleotide, an expression vector comprising said isolated polynucleotide, and a host cell transformed with said expression vector, all lack a substantial "real world" utility for the claimed invention.

Therefore, the disclosed isolated nucleotides and the isolated polypeptides encoded by said nucleotides have no well described utility other than use in further research to identify and characterize their function, and therefore the present invention fails to meet the requirement for a substantial utility as intended by the statute.

6. (A) Claims 3-8 and 11 are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial, a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention without undue experimentation.

B) Claims 3-8 and 11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while providing enablement for an isolated polynucleotide consisting of a sequence of SEQ ID NOS: 1-10 and for an isolated polynucleotide sequence that directly (with no intronic or flanking sequences) encodes a polypeptide consisting of SEQ ID NO:s 11-20 and for an isolated polynucleotide consisting of the complement, reverse complement, the reverse sequence and oligomers of SEQ ID NO:s1-10, does not reasonably provide enablement for a polynucleotide sequence with at least 40% or 60% or 75% or 90% identity with the nucleic acid sequences of SEQ ID NOS: 1-10, nor for a polynucleotide sequence that encodes a polypeptide with at least 40% or 60% or 75% or 90% identity with SEQ ID NO:s 11-20, nor for an isolated polynucleotide comprising a sequence consisting of SEQ ID NO:s 1-10, nor for an isolated polynucleotide comprising a sequence of the complement, reverse complement or the reverse sequence or oligomers of SEQ ID NO:s1-10, nor for a pharmaceutical composition of said isolated polynucleotide, an expression vector comprising said isolated polynucleotide, nor a host cell transformed with said expression vector.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, unpredictability in the art, the amount of experimentation required, and the amount of direction or guidance presented.

The specification fails to provide guidance to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation. Besides an isolated polynucleotide consisting of SEQ ID NOS: 1-10, the specification fails to provide guidance as to how to use the claimed isolated polynucleotide with at least 40% or 60% or 75% or 90% identity with an isolated polynucleotide SEQ ID NOS: 1-10, nor for a polynucleotide sequence that encodes a polypeptide with at least 40% or 60% or 75% or 90% identity with SEQ ID NO:s 11-20. Since the nucleic

acid sequence of a polynucleotide determines its protein coding properties, predictability of which changes can be tolerated in a polynucleotide's nucleic acid sequence and still retain its original functions and properties requires detailed knowledge of the ways in which the product's structure relates to its function, and detailed guidance with regard to which nucleic acids in the nucleotide sequence, if any are tolerant of modification. However, the problem of predicting functional aspects of the product from mere sequence data of a single nucleic acid sequence and what changes can be tolerated is complex and well outside the realm of routine experimentation. *In re Fisher*, 1666 USPQ 19 24 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Without such guidance, the isolated nucleotides encoding proteins possessing a disclosed property is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *Amgen, Inc. v. Chugai Pharmaceutical Co. Ltd.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991) at 18 USPQ2d 1026-1027 and *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). Therefore, there is no evidence of record to show that one skilled in the art would be able to practice the invention as claimed without an undue amount of experimentation.

The recitation of "comprising" in Claims 3-6 and their dependent claims 7-8 and 11, reads on the genes corresponding to the claimed isolated nucleotides, (especially since SEQ ID NO:s 1-10 were derived from cDNA, see the next section of this office action for a detailed explanation), which are not disclosed in the instant specification. Therefore, one of skill in the art would not know how to make said isolated polynucleotide.

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

7) Claims 3-8 and 11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

In the instant case, the specification does not convey to the artisan that the applicant had possession, at the time of invention, of the claimed

polynucleotides as recited in Claims 3-6 and 11, and of the expression vectors and host cells containing said nucleic acids and coding for a recombinant polypeptide as recited in Claims 7 and 8, and of the compositions of said polynucleotides, as recited in Claim 11.

The specification broadly describes an isolated polynucleotide of SEQ ID NO:s 1-10 that includes HnRNA which contains additional non-coding regions, genomic DNA, an entire gene or portions thereof, as well as wholly or partially synthesized polynucleotides, (see page 5 of the instant specification). Therefore, the recitation of "comprising" in Claims 3-6 and their dependent claims 7-8 and 11, reads on the genes corresponding to the claimed isolated nucleotides, especially since SEQ ID NO:s 1-10 were derived from cDNA, and said genes are not disclosed in the instant specification. The specification does not provide written description support for any 5' or 3' flanking nucleic acid sequences and/or any intronic or noncoding nucleic acid sequences of SEQ ID NOs:1-10 or of any of the recited isolated polynucleotide sequence.

The specification also broadly describes the invention as encompassing any substitution, insertion, deletion or change of nucleotides throughout the entire stretch of nucleotides found in the reference sequence by use of "% identity" recited in the claim language and disclosed in the specification (see for example pages 6-8 of the instant specification). Also depending from these sequences are the vectors, host cells and compositions of the polynucleotides of SEQ ID Nos:1-10 as broadly disclosed and recited.

According to this broad definition of isolated polynucleotides, and given the open language of *comprising* and the *% identity* language recited in the claims, none of these sequences meets the written description provision of 35 USC 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See Vas-Cath, page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath, page 1116.).

The skilled artisan cannot envision all the contemplated nucleotide

sequences by the detailed chemical structure of the claimed polynucleotides and therefore conception cannot be not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

Therefore, only an isolated polynucleotide consisting of SEQ ID NO: 1-10 and an isolated polynucleotide consisting of a nucleotide sequence encoding SEQ ID NOs:11-20, and an isolated polynucleotide consisting of the complement, reverse complement, reverse sequences and oligomeric sequences of SEQ ID NO:s 1-10, but not the full breadth of the instant claims, meets the written description provision of 35 USC 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his invention.

Claims 3, 6, 7, 8, and 11 are rejected under *35 U.S.C. § 112*, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

A) Claims 3, 6, 7, 8, and 11 are incomplete because they depend upon claim 1, which was not elected.

9. The following is a quotation of the appropriate paragraphs of *35 U.S.C. § 102* that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --
(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

10. Claims 5-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Marra et al, Accession AA184346, The WashU-HHMI Mouse EST Project, (Feb 17,1997).

Marra et al. teach an EST nucleotide sequence which comprise a 40mer, a 100mer and a 200mer of SEQ ID NO:1, (see attached Compugen sequence analysis data). Therefore, the reference teachings anticipate the claimed invention.

11. Claims 5-8 are rejected under 35 U.S.C. 102(a) as being anticipated by Marra et al, Accession AI119658, The WashU-HHMI Mouse EST Project, (Sept. 2, 1998).

Marra et al. teach an EST nucleotide sequence which comprise a 40mer, a 100mer and a 200mer of SEQ ID NO:2, (see attached Compugen sequence analysis data). Therefore, the reference teachings anticipate the claimed invention.

12. Claims 5-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Ko et al, Accession C86502 of the EST database, (Mar. 11, 1998).

Ko et al. teach an EST nucleotide sequence which comprise a 40mer, a 100mer and a 200mer of SEQ ID NO:3, (see attached Compugen sequence analysis data). Therefore, the reference teachings anticipate the claimed invention.

13. Claims 5-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Marra et al, Accession AA231415.1, The WashU-HHMI Mouse EST Project, (Feb 26, 1997).

Marra et al. teach an EST nucleotide sequence which comprise a 40mer, a 100mer and a 200mer of SEQ ID NO:4, (see attached Compugen sequence analysis data). Therefore, the reference teachings anticipate the claimed invention.

14. Claims 5-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Marra et al, Accession AA498840, The WashU-HHMI Mouse EST Project, (Jul. 1, 1997).

Marra et al. teach an EST nucleotide sequence which comprise a 40mer, a 100mer and a 200mer of SEQ ID NO:5, (see attached Compugen sequence analysis data). Therefore, the reference teachings anticipate the claimed invention.

15. Claims 5-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Marra et al, Accession AA636311, The WashU-HHMI Mouse EST Project, (Oct. 22, 1997).

Marra et al. teach an EST nucleotide sequence which comprise a 40mer, a 100mer and a 200mer of SEQ ID NO:6, (see attached Compugen sequence analysis data). Therefore, the reference teachings anticipate the claimed invention.

16. Claims 5-8 are rejected under 35 U.S.C. 102(a) as being anticipated by Marra et al, Accession AI050489, The WashU-HHMI Mouse EST Project, (Jul. 9, 1998).

Marra et al. teach an EST nucleotide sequence which comprise a 40mer, a 100mer and a 200mer of SEQ ID NO:7, (see attached Compugen sequence analysis data). Therefore, the reference teachings anticipate the claimed invention.

17. Claims 5-8 are rejected under 35 U.S.C. 102(a) as being anticipated by Marra et al., Accession AA921460, The WashU-HHMI Mouse EST Project, (Apr. 20, 1998).

Marra et al. teach an EST nucleotide sequence which comprise a 40mer, a 100mer and a 200mer of SEQ ID NO:8, (see attached Compugen sequence analysis data). Therefore, the reference teachings anticipate the

claimed invention.

18. Claims 5-8 are rejected under 35 U.S.C. 102(a) as being anticipated by Marra et al., Accession AA466595 and AI287088, The WashU-HHMI Mouse EST Project, (March 9, 1999 and Nov. 24, 1998, respectively).

Marra et al. teach an EST nucleotide sequence which comprise a 40mer, a 100mer and a 200mer of SEQ ID NO:9, (see attached Compugen sequence analysis data). Therefore, the reference teachings anticipate the claimed invention.

19. Claims 5-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Marra et al., Accession W77540, The WashU-HHMI Mouse EST Project, (Jun 20, 1996).

Marra et al. teach an EST nucleotide sequence which comprise a 40mer, a 100mer and a 200mer of SEQ ID NO:10, (see attached Compugen sequence analysis data). Therefore, the reference teachings anticipate the claimed invention.

20. Claims 3, and 7-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Mariage-Sampson R et al, Genome Res., 6:492-503, (1996).

Mariage-Sampson et al teach a nucleotide sequence which encodes a polypeptide having at least 40% identical residues to SEQ ID NO:16, according to a compugen search (See entire article). Therefore, the reference teachings anticipate the claimed invention.

21. Claims 3, and 7-8 are rejected under 35 U.S.C. 102(a) as being anticipated by Agostino et al, WO9849302A1, (Nov. 1998).

Agostino et al. teach a nucleotide sequence which encodes a polypeptide having at least 40%, 60 and 75% identical residues to SEQ ID NO:17, according to a compugen search. Therefore, the reference teachings anticipate the claimed invention.

22. Claims 3, and 7-8 are rejected under 35 U.S.C. 102(a)/(e) as being anticipated by Ruben et al, WO9910364A1, (March 4,1999) and or U.S. Patent No. 5,942,420.

Ruben et al. and '420 teach a nucleotide sequence which encodes a polypeptide having at least 40% and 60% identical residues to SEQ ID NO:20, according to a compugen search. Therefore, the reference teachings anticipate the claimed invention.

23. Claims 5-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Marra et al., Accession AA646983, The WashU-HHMI Mouse EST Project, (Oct. 28, 1997).

Marra et al. teach a nucleotide sequence having at least 40% identical residues to SEQ ID NO:1, (see attached Compugen sequence analysis data). Therefore, the reference teachings anticipate the claimed invention.

24. Claims 5-8 are rejected under 35 U.S.C. 102(a) as being anticipated by Yaspo et al, Genomics 49:133-136 (April 1,1998).

Yaspo et al. teach a nucleotide sequence having at least 40% identical residues to SEQ ID NO:2, (see attached Compugen sequence analysis data). Therefore, the reference teachings anticipate the claimed invention.

25. Claims 5-8 are rejected under 35 U.S.C. 102(a) as being anticipated by Marra et al., Accession AI119658, The WashU-HHMI Mouse EST Project, (Sept. 2, 1998).

Marra et al. teach a nucleotide sequence having at least 40%, 60% and 75% identical residues to SEQ ID NO:2, (see attached Compugen sequence analysis data . Therefore, the reference teachings anticipate the claimed invention.

26. Claims 5-8 are rejected under 35 U.S.C. 102(a) as being anticipated by Ko et al, Accession C86502 of the EST database, (Mar. 11, 1998).

Ko et al. teach an EST nucleotide sequence having at least 40% and 60% identical residues to SEQ ID NO:3, (see attached Compugen sequence analysis data . Therefore, the reference teachings anticipate the claimed invention.

27. Claims 5-8 are rejected under 35 U.S.C. 102(a) as being anticipated

by Pietu et al., Biochem J. 335 (Pt.3):549-556, (Nov. 24, 1998).

Pietu et al. teach a nucleotide sequence having at least 40% identical residues to SEQ ID NO:6, (see attached Compugen sequence analysis data. Therefore, the reference teachings anticipate the claimed invention.

28. Claims 5-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Marra et al., Accession AA116725, The WashU-HHMI Mouse EST Project, (Feb. 13, 1997).

Marra et al. teach a nucleotide sequence having at least 40% identical residues to SEQ ID NO:7, (see attached Compugen sequence analysis data). Therefore, the reference teachings anticipate the claimed invention.

29. Claims 5-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Marra et al., Accession AA475668, The WashU-HHMI Mouse EST Project, (Jun. 18, 1997).

Marra et al. teach a nucleotide sequence having at least 40% identical residues to the complement of SEQ ID NO:7, (see attached Compugen sequence analysis data). Therefore, the reference teachings anticipate the claimed invention.

30. Claims 5-8 are rejected under 35 U.S.C. 102(a) as being anticipated by Marra et al., Accession AI287088, The WashU-HHMI Mouse EST Project, (Nov. 24, 1998).

Marra et al. teach a nucleotide sequence having at least 40% identical residues to SEQ ID NO:9, (see attached Compugen sequence analysis data). Therefore, the reference teachings anticipate the claimed invention.

31. Claims 5-8 are rejected under 35 U.S.C. 102(e) as being anticipated by Holtzman et al., U.S. Patent No. 5942420.

Holtzman et al. teach a nucleotide sequence having at least 40% identical residues to SEQ ID NO:10, (see attached Compugen sequence

analysis data). Therefore, the reference teachings anticipate the claimed invention.

32. Claims 5-8 are rejected under 35 U.S.C. 102(a) as being anticipated by Yaspo et al, Genomics 49:133-136 (April 1,1998).

Yaspo et al. teach a nucleotide sequence having at least 40% and 60% and 75% identical residues to SEQ ID NO:12, (see attached Compugen sequence analysis data). Therefore, the reference teachings anticipate the claimed invention.

33. No claim is allowed.

34. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy DeCloux whose telephone number is (703) 306-5821. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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April 18, 2000

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